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The Benefits of Adequate Iodine Intake

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In past decades, researchers in various countries have studied the consequences of iodine deficiency on the mental and physical development of children and adults. Iodine deficiency proved to have disastrous consequences on cognitive and psychomotor development for a limited group (i.e., DeLong 1989). These are the so-called cretins, who make up more than 10% of the population in some areas. The World Health Organization estimates the worldwide number of overt cretins at around 5.7 million (Hetzel 1994).

Outcomes of study of the effects of iodine deficiency on the development of the noncretinous portion of a population living in an iodine-deficient area are less clear cut. While some studies pointed to a strong negative effect, little or no effect was found in others.

To obtain an overall picture of the current state of knowledge, the first part of this paper summarizes the results of a great many studies that have been performed in recent years. All these studies involved a comparison of the mental and psychomotor development in two groups of children and/or adults: (1) a non-iodine-deficient group — people living in a non-iodine-deficient area or children whose mothers were injected with iodized oil in the first part of their pregnancy; and (2) an iodine-deficient group — people living in an area with a serious iodine deficiency. Meta-analysis was used to combine the results of the studies.

In the second part of this paper, the outcomes are discussed of a recent study of the effect of iodine supplementation on the mental and psychomotor development of children born and raised in an iodine-deficient area in Malawi (Shrestha 1994). Although very little research has been done in this field, it is of great importance to know whether the negative effects of iodine shortage can be corrected at a later age through iodine supplementation.

Meta-analysis

The method of meta-analysis makes it possible to integrate the outcomes of a large number of studies on a single topic, resulting in a single overall estimate of the effect under study. This overall estimate is the average of the various outcomes weighted for sample size (Wolf 1986), whereby studies that used larger groups of subjects are ascribed more weight than studies performed on smaller groups.

This overall estimate, termed the "population effect size," can be taken seriously only when the studies on which it is based meet the "homogeneity criterion": the outcomes of the individual studies must not be too greatly divergent. Stoffelmayer et al. (1983) developed a measure for the degree of heterogeneity.

A meta-analysis consists of six steps: formulating the research issue, selecting the studies, coding characteristics of the studies, statistical analyses, interpreting the results, and drawing conclusions. The present study used the meta-analysis program of Schwarzer (1989).

Objectives

The objective of the meta-analysis is twofold. In the first place, it provides a highly complete summary of the research that has been performed in recent years on the relationship between iodine deficiency and mental and psychomotor development. Because the outcomes of the various studies are converted into the same measure, it is much

Table 1. Psychomotor ability: studies included in the meta-analysis

Country	*n*	Age (y)	Test	*r*
Italy	250	6–12	Bender Gestalt Test	.48
Indonesia	143	6–12	Bender Gestalt Test	.37
Spain	97	2.5–5	McCarthy Motor Development Scale	.34
Zaïre	75	4–23[a]	Brunet-Lezine Scale	.30
Spain	78	6–8	Bender Gestalt Test	.29
Ecuador	264	8–18	Goddard Test for Psychomotor Development	.25
Chili	90	6–12	Bender Gestalt Test	.13
Spain	156	9–2	Bender Gestalt Test	.13
Bolivia	200	5.5–12	Bender Gestalt Test	-.01
Spain	74	2–30[a]	Bayley Scale of Infant Development (motor)	-.03

[a] Age in months.

easier to obtain a clear picture of the extent to which the results agree. In the second place, the combined studies yield an estimate of the overall effect of iodine deficiency on the mental and psychomotor development of people who live in an iodine-deficient area.

Study Design

To make it possible to replicate and verify the study, the meta-analysis only included studies that had been reported in books (proceedings), journals, IDD newsletters, and theses.

Some of the studies involved the influence of iodine deficiency on psychomotor functioning. In that case, meta-analysis was performed not only for psychomotor functioning in general but also for more specific psychomotor skills. Based on factor-analytic study (Bleichrodt et al. 1989) and on research by Fleishman (1972) of skill clustering within the psychomotor domain, three factors were distinguished: manual dexterity, speed of reaction and coordination of movements. Other studies involved the influence of iodine deficiency on mental development. The results of the meta-analysis of these studies were previously published in *The Damaged Brain of Iodine Deficiency* (Stanbury 1994). We will therefore limit ourselves to a few of the most important outcomes of this meta-analysis.

All studies involved different groups of people. If more than one test was administered to the same group, then prior to meta-analysis these scores were combined into a single score.

Some studies used test instruments that were developed specifically for the culture in question to determine mental and psychomotor development. More often, however, translations or adaptations of instruments from other, generally Western, cultures were used.

If a study is to be used in a meta-analysis, data must be known on the number of persons who participated in the study, the types of tests used, the independence of the study groups, and an indication (t, F, r, χ^2, or average and standard deviation) of the differences in test results between the iodine-deficient and non-iodine-deficient groups. Using transformation formulas, these different indices are converted into a single measure, the Pearson correlation coefficient.

Results

Table 1 shows the studies that focused on general psychomotor functioning. A total of 10 studies performed in seven different countries qualified for the meta-analysis. The test most frequently used was the Bender Gestalt test or adaptations of it (Koppitz 1975). A total of 1427 persons ranging in age from 2 months to 18 years were studied.

The effect sizes, given in correlation coefficients (r), showed much variation, from +.48 to -.03. The degree of homogeneity of the studies was determined using the index developed by Stoffelmayer et al. (1983). Together, the 10 studies did not meet the homogeneity requirement, which meant that they had not been performed on the same population.

When the two studies with a negative effect size, the studies in Spain and Bolivia, were omitted, the remaining eight studies, including 1153 individuals, were homogeneous. By transforming the outcomes into Fisher z-scores, an estimate could be made of the population effect size (weighted mean r). This was done using the Schmidt-Hunter method (Schwarzer 1989) in which different weights are ascribed to the various studies on the basis of the size of the groups studied. The weighted population effect size calculated was .30 (p<.00000), with a 95% confidence interval from .25 to .35 (see **Table 2**).

The studies relating to more specific factors within the psychomotor domain are shown in **Table 3**. Unfortunately, the number of these studies is limited, especially for the factors "speed of reaction" and "coordination of movements."

As the seven studies involving research of manual dexterity formed a homogeneous group, it was not necessary to leave out any studies for the calculation of the overall effect size. The total number of individuals who took part in these studies was 1859. The weighted population effect size was .41 (p<.00000), and the 95% confidence interval was between .37 and .45.

The effect sizes calculated for the "speed of reaction" factor were quite divergent. The two studies in China showed the most extreme effect sizes of .74 and -.05, and they were consequently omitted in calculating the overall index. The weighted population effect size here was .26,

Table 2. Results of the meta-analyses for psychomotor and cognitive abilities

Variables	Psychomotor ability: General	Manual dexterity	Speed of reaction	Coordination of movements	Cognitive ability
Number of studies	8	7	3	3	18
Number of subjects	1153	1859	429	429	2214
Population effect size	.30	.41	.26	.11	.40
Significance	.000	.000	.000	.009	.000
Mean standardized difference	.66	.96	.55	.22	.90
95% confidence interval	.25–.35	.37–.45	.17–.35	.02–.20	.36–.43

with a 95% confidence interval from .17 to .35.

The three studies relating to the "coordination of movements" factor yielded an overall effect size of .11 and a 95% confidence interval from .05 to .20.

Table 4 summarizes the 21 studies on the relationship between iodine deficiency and cognitive development. To obtain a homogeneous group of studies, the three studies with the smallest effect sizes were not used for meta-analysis. The effect sizes for the remaining 18 studies, with a total of 2214 individuals, ranged from .18 to .57. The weighted population effect size was .40 (significant at $p<.00000$), with a 95% confidence interval from .36 to .43.

Figure 1 shows all effect sizes with the corresponding 95% confidence intervals.

Table 3. Dimensions of psychomotor ability: studies included in the meta-analysis

A. Manual dexterity

Country	*n*	Age (y)	Test	*r*
Indonesia	102	13–20	Tapping	.48
China	936	8–14	Tapping	.47
China	120	8–14	Tapping	.45
China	87	8–14	Tapping	.45
Indonesia	143	6–12	Tapping, Pinboard	.39
Spain	184	6–12	Tapping, Pinboard, Making dots, Threading beads	.31
Spain	287	6–12	Making dots, Threading beads	.20

B. Speed of reaction

Country	*n*	Age (y)	Test	*r*
China	87	8–14	Simple reaction time	.74
Indonesia	102	13–20	Simple and choice reaction time	.41
Indonesia	143	6–12	Simple and choice reaction time	.22
Spain	184	6–12	Simple and choice reaction time	.20
China	120	8–14	Simple reaction time	-.05

C. Coordination of movements

Country	*n*	Age (y)	Test	*r*
Indonesia	143	6–12	Throwing balls, balance	.20
Indonesia	102	13–20	Throwing balls, balance	.05
Spain	184	6–12	Throwing balls, balance	.05

Effects of Iodine Supplementation

So far, very little research has been done of the effects of iodine supplementation on mental and psychomotor development of people living in an iodine-deficient area. A few years ago, one such study was started by the Department of Human Nutrition of Wageningen Agricultural University. The study, doctoral research by Ramesh Shrestha, was performed in the Ntcheu district in Malawi, an iodine-deficient area where 86% of the children "were at least moderately iodine-deficient with urinary iodine concentrations below 0.4 μmol/L and 18% were anemic (blood hemoglobin concentration <110 g/L)". The Free University of Amsterdam and the Tilburg University, both in the Netherlands, were also involved in this study.

Study Design

The research group consisted of a total of 321 children aged from 6 to 8 years from three primary schools. The children were divided into four groups that were controlled for school class, age, and sex:

1. placebo group (n=82)
2. iodine-supplemented group (n=79)
3. iron-supplemented group (n=78)
4. iodine- plus iron-supplemented group (n=82)

This publication will report outcomes only from the study of the first two groups of children, the placebo group and the iodine-supplemented group.

Both groups of children were given a large number of tests to determine their cognitive and psychomotor skills. The tests were administered twice: immediately before the children were given iodized oil and poppyseed oil, and 10 months afterward. As it was a double-blind study, the teachers and the researchers learned only after the tests were administered for the second time which children had been treated with iodine and which children had been in the placebo group.

Test Battery

Psychomotor abilities. The following tests were selected to study the psychomotor aspects:

Table 4. Cognitive ability: studies included in the meta-analyses

Country	*n*	Age (y)	Test	*r*
Indonesia	102	13–20	Test Intelligensi Kollektip Indonesia	.57
New Guinea	20	10–12	Pacific Design Construction Test	.56
Spain	97	2.5–5	McCarthy Scales of Children's Abilities	.53
China	499	7–14	Combined Raven's Test for Rural China.	51
Ecuador	32	3–5	Stanford-Binet Intelligence Scale	.50
Ecuador	46	6–10	Goodenough Draw-a-Man Test	.48
Ecuador	67	3.5–5.5	Stanford-Binet Intelligence Scale	.48
Spain	184	6–12	Cattell Culture Fair Intelligence Test	.45
Ecuador	124	3.5–5.5	Stanford-Binet Intelligence Scale	.37
Indonesia	143	6–12	Test Intelligensi Anak	.36
Spain	74	2–30[a]	Bayley Scale of Infant Development	.36[c]
China	192	7–14		.28
China	99	25–45		.28
Indonesia	163	5–20	Raven Coloured Progressive Matrices	.28
Zaire	138	4–23[a]	Brunet-Lézine Scale	.26
Ecuador	50	6–10	Goodenough Draw-A-Man Test	.24
Chili	90	±6–±12	Wechsler Intelligence Scale for Children Rev.	.20
China	94	0–7		.18
Ecuador	108	12–15	Wechsler Intelligence Scale for Children	.12
Ecuador	154	8–12	Stanford-Binet Intelligence Scale	.08
Bolivia	200	5.5–12	Stanford-Binet Intelligence Scale	.04

Source: Bleichrodt and Born (1994).
[a] Age in months.

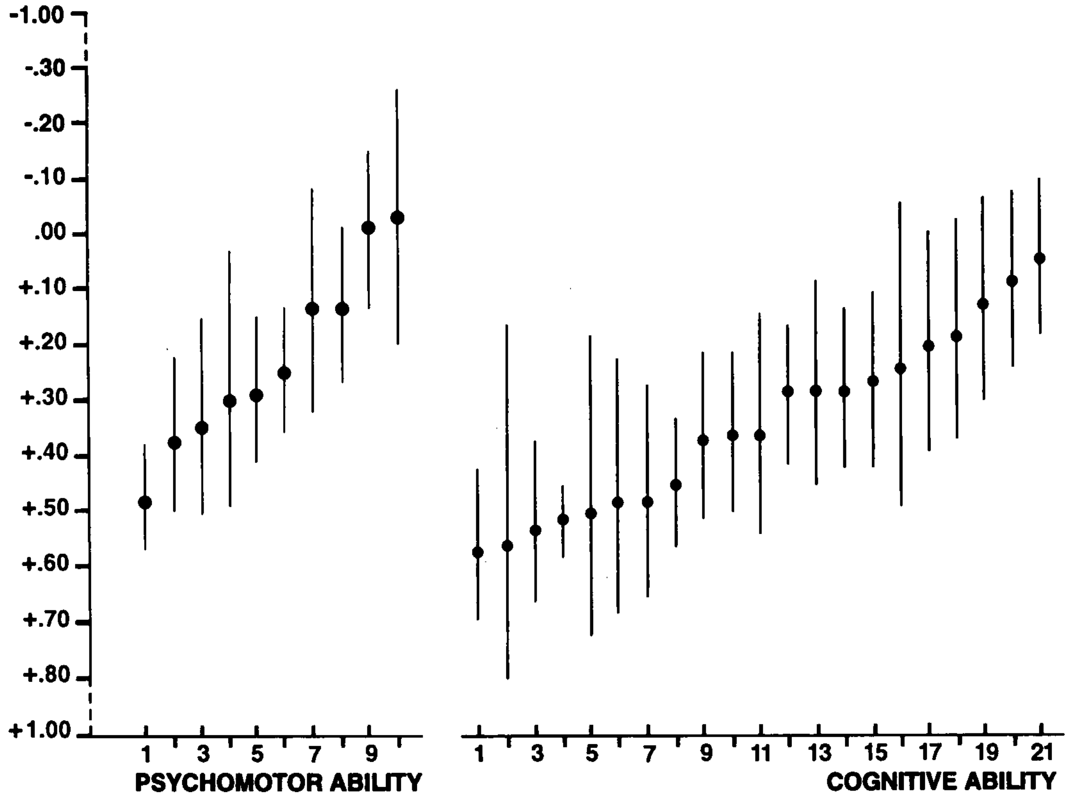

Figure 1. Visual display of effect sizes and confidence intervals for 10 studies concerning psychomotor ability and 21 studies concerning mental ability

1. Pegboard: inserting pegs into holes as quickly as possible
2. Tapping: tapping two hatched rectangular plates with a pencil as rapidly as possible
3. Throwing balls: throwing balls into a basket from a fixed distance
4. Balancing: standing on each foot for as long as possible with a maximum of three minutes
5. Sitting/standing: sitting down and standing up as many times as possible in one minute
6. Reaction time: pressing a button as soon as a small square appears on a screen and a beep is heard
7. Handgrip: hand muscle strength measured by means of a hand dynamometer

The same or comparable tests have been used in previous research of the effects of iodine deficiency on psychomotor development. Although the test battery does not represent the full spectrum of the psychomotor domain, it does cover important aspects such as finger and manual dexterity, eye-hand coordination, reaction time, and coordination of movements.

Cognitive abilities. The choice of the tests to determine cognitive abilities was based on the nonhierarchical multifactor model of Thurstone (1938). Even today, the factors identified by Thurstone — verbal, numerical, spatial, perceptual, word fluency, memory, and reasoning — are still considered to be important distinctions in intelligence theory, and they are therefore represented in many test batteries. This also applies to the test battery used for the research in Malawi. The test battery consisted of six subtests:

1. Fluency: giving as many names of persons and animals as possible within a certain time limit
2. Exclusion: indicating which of four objects or abstract figures does not satisfy the same condition as the other three
3. Quantity: making comparisons in number, volume, length, distance, weight, surface area, etc., on the basis of drawings
4. Verbal meaning: from four pictures, choosing the one that corresponds to the word named by the tester
5. Visual memory: recognizing a figure shown earlier among a group of several figures
6. Closure: recognizing objects which are shown in an incomplete fashion

Previous study has shown that the psychological meaning of the above tests is comparable for different cultures.

On the basis of the six subtest scores a total score was calculated as an indication of overall cognitive functioning. However, the reliability of the individual subtests also allowed their separate analysis and interpretation.

Results

Figure 2 shows the differences in test scores between the iodine-deficient or placebo group and the non-iodine-deficient or treated group. The differences are expressed as d-values. The d-value is the difference between the means of the two groups divided by the standard deviation. Cohen (1988) divided the d-values into three categories: small effect size (d=0.2), medium effect size (d=0.5), and large effect size (d=0.8).

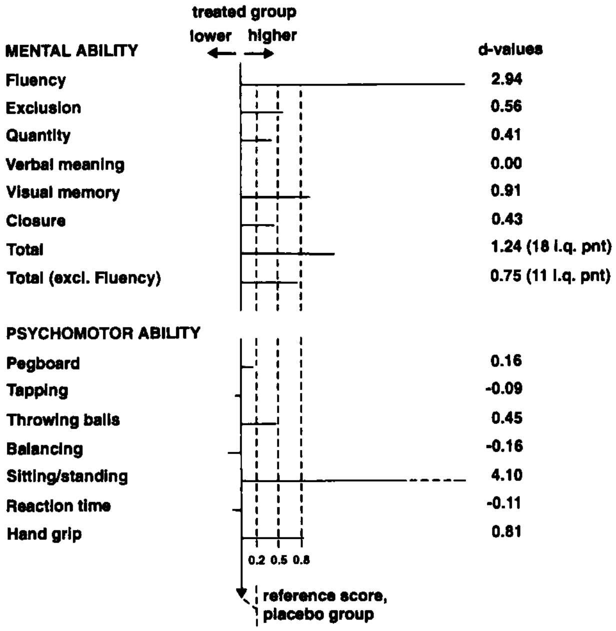

Figure 2. Differences in test scores between the iodine-treated group and the placebo group expressed in d-values.

The outcomes of the research of the effects of iodine supplementation on psychomotor development in the children studied were not clear-cut. For skills measured by the subtests Pegboard, Tapping, Balancing, and Reaction time, the effects were negligible. A medium effect size was found for Throwing balls, while a large effect size was found for Handgrip and, even more pronounced, for Sitting/standing.

The outcomes for the mental abilities were clearer. With the exception of the subtest Verbal meaning, with a d-value of zero, positive d-values were found, ranging from medium effect sizes for Exclusion, Quantity, and Closure to large effect sizes for Fluency and Visual memory.

Together the six subtests give a reliable indication of the general cognitive functioning of the children. The d-value of 1.24 is very high: concretely, it means a difference of 1.24 SD or 18 IQ points between the group that received supplemental iodine and the placebo group. If the extremely high d-value for Fluency is left out, the other five subtests still show a d-value of 0.75, or a difference of 11 IQ points.

Conclusion and Discussion

There is great variation in the outcomes of the studies that focused on psychomotor skills. Even when the same test was used, the effect sizes found differ greatly from study to study; for example, the correlation coefficients for the

Bender Visual Motor Gestalt Test vary from -.01 to .48 and for the Reaction time test from -.05 to .74. However, the group of subjects with an iodine deficiency obtained lower scores than the group that did not suffer from an iodine deficiency in nearly all studies.

Table 5. Summary meta-analyses and Malawi study

Test	Meta-analysis (d-value)[a]	Malawi study (d-value)[b]
Psychomotor ability		
General	.66	.25
Manual dexterity	.96	.07
Speed of reaction	.55	-.11
Coordination of movements	.22	.29
Muscle strength	—	2.46
Cognitive ability		
General	.90 (13 IQ points)	1.24 (18 IQ points) 0.75 (11 IQ points)[c]

[a] Difference between iodine deficient/non-iodine-deficient.
[b] Effect of iodine supplementation.
[c] Excluding Fluency.

Table 5 summarizes the outcomes of the meta-analyses and Malawi study. The highest difference was found for skills requiring manual dexterity (Pegboard, Tapping), for which a high *d*-value of 0.96 was found (large effect size). For the factor of Reaction time and for general psychomotor functioning, *d*-values were found of 0.55 and 0.66 respectively (medium effect size).

Assuming that the outcomes of the meta-analyses are reliable, then on the basis of the outcomes of the Malawi study, we must conclude that the disorders in psychomotor development that are caused by an iodine deficiency cannot be corrected, at least not within the 10 months that the study lasted in Malawi. The differences between the group that was treated with iodine and the nontreated (placebo) group are negligible; the *d*-values for the psychomotor skills range from -0.11 to 0.15. Iodine supplementation seems to give an improvement only for the factor of muscle strength, where a large effect size was found.

The studies that focused on the influence of iodine deficiency on cognitive development yield a fairly straightforward picture. The correlation coefficients vary from .04 to .57, with a median of .36. The *d*-value is 0.90 (large effect size), which means a difference of 13 IQ points between the iodine-deficient and the non-iodine-deficient group. However, from the results of the study in Malawi, we may conclude that iodine supplementation can make up for developmental lag of the iodine-deficient group within a year: the *d*-value of 1.24 found for general cognitive ability implies that the average test score of the treated group is roughly 18 IQ points higher. Even when the subtest most susceptible to environmental factors, Fluency, is omitted, a considerable difference of 11 IQ points remains between the two groups.

The remarkable outcomes of both the meta-analysis and the Malawi study point to the need for further research. Some factors that will require special attention are the choice of the research groups, the selection of the test instruments, and the control of the conditions under which the tests are administered.

As much as possible, test batteries for both psychomotor skills and cognitive skills must be composed of tests that are culture fair. When the tests are administered, much attention should be paid to aspects such as standardization and objectivity. Administrating the same test in several different countries will yield important information on the effects of iodine deficiency on psychomotor and cognitive development and the effects on development if iodine is administered at a later age.

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